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Feasibility and Safety of Early Exercise Testing Using the Bruce Protocol After Acute Myocardial Infarction

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OBJECTIVES To assess the feasibility and safety of exercise testing (ET) using a Bruce protocol (BPR) within three days of an acute myocardial infarction (AMI) with the data obtained from a prospectively managed database.

BACKGROUND Exercise testing after AMI is usually done between days 4 and 6 and often using a "low-level" protocol. Earlier testing with BPR may allow for efficient triage.

METHODS Patients were considered for early ET when off intravenous nitroglycerine with no rest angina, uncontrolled cardiac failure or arrhythmias.

RESULTS Of 300 consecutive AMI patients who underwent an ET, 216 (72.0%; M = 163, F = 53; age mean 59 ± 0.8 SEM, range 34 to 83 years) had ET within three days of admission. There were 124 (57%) negative, 56 (26%) positive and 36 (17%) indeterminate tests. The maximum heart rate achieved was 116 ± 1 beats/min (range 64 to 163), which was 72.2 ± 0.8% of predicted maximum (86.6% on beta-adrenergic blocking agents at ET; exercise duration = 6.7 ± 0.2 min). Reasons for termination: maximum effort—89 (41%); low-level test target (stage III/IV of BPR)—63 (29%); positive ST segment change—19 (9%); severe chest pain—12 (5.5%); reaching 90% predicted maximum heart rate—6 (3%); nonsustained ventricular tachycardia—1 (0.5%); other—26 (12%). Fourteen (6.5%) patients had minor complications (i.e., drop in systolic pressure, chest pain >5 min) with no cardiac arrests, AMIs or deaths. After the ET, 87 (40%) patients were discharged the same day, 73 (34%) the next day.

CONCLUSIONS The majority of ETs after an AMI can be done using the Bruce protocol within three days of admission with a very low incidence of complications. This can lead to early triage and potential cost savings. (J Am Coll Cardiol 2000;35:1212–20) © 2000 by the American College of Cardiology

Although the incidence of coronary artery disease has been decreasing in developed countries over the last two to three decades, the prevalence is expected to increase given the rapid aging of the population (1). Acute myocardial infarction (AMI) remains the first clinical manifestation of coronary artery disease in a significant proportion of patients. The occurrence of an AMI has considerable influence on short-term as well as long-term morbidity and mortality (2,3). Even though mortality during the first year after an AMI remains relatively low (approximately 10%), about 40% to 50% of the patients experience a significant coronary event (reinfarction, need for revascularization, development of congestive cardiac failure) during this period (4). Further, a majority of these coronary events appear to be concentrated within the first six weeks to three months after the AMI, making early identification of these patients a priority to hopefully alter this prognosis favorably (4). Although limitations exist, exercise testing (ET) has remained the most universally available method for the initial prognostication of patients with an AMI. Further, the goals and needs of ET as well as the population that requires ET may have undergone changes over the last 10 to 15 years because of increasing utilization of thrombolytic therapy, primary angioplasty or early postinfarction coronary angiography/angioplasty before exercise testing. Generally ET is done approximately the fifth to eighth day after AMI after a graduated program of mobilization initially within the coronary/intermediate care units (CICUs) followed by a period on the medical ward (5,6). A recent review on ET has listed an AMI within the preceding three to five days as an absolute contraindication to exercise testing (5). Further, the American College of Cardiology/American Heart Association guidelines for ET considers the "safety of ET"

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Abbreviations and Acronyms

AMI = acute myocardial infarction
BPR = Bruce protocol
CABGP = coronary artery bypass surgery group
CAGP = coronary angiography/angioplasty group
CK-MB = creatine kinase isoenzyme–myocardial band
CICU = coronary/intermediate care unit
DECGP = deceased group
ECG = electrocardiogram
EETGP = early exercise test group
ET = exercise test/testing
LETGP = late exercise test group
NETGP = no exercise test group
URV = unscheduled return visits

performed within three days after an AMI as not being established (7). However, there has been increasing pressure in terms of minimizing the durations of hospital stay for all acute illnesses including AMI due to budgetary constraints within the health care systems. If one is to continue with a noninvasive assessment for risk stratification (to select patients for coronary angiography) in this era, one of three strategies can be adopted: 1) early discharge followed by ET as an outpatient over the ensuing two to six weeks, 2) ET done very early after an AMI after a strategy of accelerated mobilization of the patients, 3) pharmacologic stress testing with dipyridamole-sestamibi imaging or dobutamine-stress echocardiography. Although the third approach is likely to offer the best sensitivity and specificity, it is more costly and not universally available at short notice. The first approach is safe (from the ET point of view) and feasible, but the major disadvantage remains the early occurrence of coronary events after an AMI (4). Thus, if one were to utilize the ET as a means of identifying those who are likely to have events, in the hope of minimizing their occurrence, postponing the test could be detrimental. This is due to the fact that arranging outpatient coronary angiography (to hopefully consider revascularization to prevent these events in those with positive ET) will involve more delays (in most countries) than if the procedure was performed before discharge at the time of the index infarction. Thus, the strategy of very early ET will be preferred whenever feasible. A handful of studies are available on the feasibility and safety of ET within the first three to four days of an AMI, but the patients selected in these studies have been mostly individuals who have undergone coronary angiography (and revascularization if necessary) before the ET (8). However, one could argue that this constitutes the very group where an ET would provide the least amount of information needed for patient management. This is because the main objective of doing an ET (i.e., to consider coronary angiography) has already been dealt with in this category of patient. In addition, it is likely that after revascularization, an ET would likely result in less complications.

Since 1995 at this institution an attempt has been made to discharge patients with AMI directly from the coronary care unit (9). In pursuit of this goal, an attempt is made to perform ETs very early after the AMI to assist in risk stratification and to decide on the feasibility of early discharge or the need for in-hospital coronary angiography. This investigation is an observational study with the data obtained from a prospectively managed database.

METHODS

All patients admitted with an AMI from July 1996 to October 1998 were included in this study. Clinical, investigational and demographic data on all patients admitted to the CICU were collected prospectively. The constitution of the database has been described previously (9). The diagnosis of an AMI was made based on the presence of at least two of the following three criteria: 1) chest pain suggestive of myocardial ischemia lasting 30 min or longer, 2) enzymatic evidence of acute myocardial necrosis, as demonstrated by a rise in creatine kinase levels with the creatine kinase isoenzyme–myocardial band (CK-MB) fraction being greater than 5%, 3) new electrocardiographic change which included development of Q waves or ST/T changes lasting 48 h or longer.

All patients with an AMI were considered as candidates for direct discharge from the CICU with their mobilization done in an accelerated manner. The following were used as a guide to selecting patients for early ET: 1) absence of chest pain/dyspnea on walking in the CICU on telemetry, 2) absence of New York Heart Association class III/IV congestive cardiac failure, 3) absence of recurrent nonsustained ventricular tachycardia, 4) absence of atrial fibrillation with an uncontrolled ventricular response with ambulation within the CICU. Those patients who had ET done within the first 3 days of their AMI were included in the study. However, comparison was made between this group of patients and all the other patients with an AMI who were admitted during the same time period. The patients were divided into five groups: 1) early ET group (EETGP)—those patients who had ET done within 72 h of the time recorded in the hospital admission form, 2) late ET group (LETGP)—those patients who had ET done after three days but before hospital discharge, 3) coronary angiography/angioplasty group (CAGP)—those patients who did not have an ET as they had coronary angiography/angioplasty done due to continuing angina before consideration of an ET, 4) coronary artery bypass surgery group (CABGP)—those patients who underwent coronary angiography because of continuing angina before consideration of an ET followed by coronary artery bypass surgery during their hospital stay, 5) deceased group (DECGP)—those patients who died during their hospital stay before an ET being done, 6) no ET group (NETGP)—the patients who were discharged home without a predischarge ET as they were not deemed as able to walk on a treadmill due to reasons

such as poor physical mobility, lightheadedness, or dyspnea on walking on level ground. There were some patients in the EETGP and LETGP who underwent coronary angiography with or without revascularization after an abnormal ET. In the CAGP a predischarge ET after the angiography/angioplasty was considered superfluous, and, thus, an outpatient ET was arranged four to six weeks after discharge.

All patients had ET using an automated system (model # Q5000, Quinton Instruments Company, Bothell, Washington). The electrocardiogram (ECG) (12-lead) was recorded using the lead system described by Mason and Likar (10). A 12-lead ECG was recorded before exercise, at the end of each stage of exercise, at end of exercise and 1 min, 2 min and 4 min after completion of the exercise. Leads V3, V5 and aVF were monitored continuously with the magnitude of ST segment depression measured 80 ms after the J-point and the ST segment slope analyzed. Horizontal/downsloping nett ST segment depression of >0.1 mV observed in three consecutive beats was considered a positive test (irrespective of the presence/absence of chest pain). The final results were tabulated as being positive, negative or indeterminate. The tests that were not positive together with a maximum heart rate achieved of $<70\%$ of the predicted maximum or completion of <6 min on the Bruce protocol (BPR) were considered indeterminate. The following end points were utilized for termination of the test: 1) horizontal or downsloping ST depression in excess of 0.2 mV (test terminated before this in the presence of concomitant chest pain, typical of angina, associated with horizontal or downsloping ST depression >0.1 millivolts); 2) fall in systolic blood pressure of >10 mm Hg accompanied by symptoms of lightheadedness; 3) sustained ventricular tachycardia or frequent runs of nonsustained ventricular tachycardia; 4) as requested by the patient, although encouragement was given to continue whenever no other reason for termination was apparent; 5) at the end of stage IV of the BPR in those patients <60 years of age and at the end of stage III of the BPR in those patients >60 years of age; 6) achieving 90% of the predicted maximum heart rate for age; 7) maximum effort.

Follow-up. The postdischarge course was evaluated six weeks after discharge by a telephone interview using a structured questionnaire. All attempts were made to contact the patients at home or at work. Confirmation of readmissions during the six-week postdischarge period was obtained from discharge summaries. Visits to the physicians arranged at the time of discharge were regarded as scheduled visits. All other visits to physicians, together with all readmissions, were categorized as unscheduled return visits (URV). All patients were also contacted at approximately one year after hospital discharge.

Statistical analysis. All data were entered into a database formulated within the SPSS data management systems. Continuous variables were entered as such with all discrete variables categorized to ensure that responses would fall into mutually exclusive categories. The cross-tabulations were done on discrete variables using a chi-square test. Analyses on continuous variables were made using a one-way analysis of variance. The least significance difference test was used to determine the statistical significance of differences between groups whenever the F value was significant. A p value of <0.05 is quoted for all analyses, accepting the limitation of this value with multiple comparisons that are inherent in any observational study. Thus, the p value by itself should not be accepted as demonstrating a clinically significant difference between groups.

The follow-up data between the groups was analyzed using an analysis of variance. After this, the significance of the differences between individual groups was made using Bonferonni's intervals to make allowances for multiple comparisons (this was done whenever the F value was significant). A discriminant function analysis was carried out to determine whether the individuals who died within a year of discharge could be identified at the time of discharge. The details of the methodology has been described previously (4). In summary, all variables considered as having a possible impact on posthospital mortality were entered into a stepwise discriminant function analysis program to obtain the best possible discrimination between the two groups (i.e., one year death vs. no death). During the analysis the variables were entered in a stepwise manner to obtain the best possible discrimination. At each step, a single additional variable was entered into the set of discriminating variables. The variables entered were selected on the basis of minimizing the overall Wilk's lambda, a generalized distance measure. The program calculated the canonical correlation for the discriminant function and the canonical discriminant function coefficients for each of the discriminating variables.

The program also classified each patient into one of the two groups (one year death vs. no death) using the "Jackknife" method of Lachenbruch (11). In this method, a single patient is removed, and the discriminant function analysis is carried out on the remaining $(n - 1)$ patients. The resulting discriminant function equation is then applied to the data from the removed patient to predict the group (one year death or no death) to which the patient belongs. This analysis was performed sequentially on each patient and the predicted group compared with the actual group in each case. This method provides a relatively unbiased estimation of the error rate of the discriminant function analysis (11).

RESULTS

During the period of the study there were 540 patients admitted with a diagnosis of AMI. There were 374 (69.3%) men and 166 (30.7%) women with a mean age of 64.7 ± 0.6 years (standard error of the mean). Two hundred and sixteen (40.0%) patients received thrombolytic therapy with alteplase or reteplase given in 132 (61.1%) patients and streptokinase in 74 (34.3%) patients. The location of the

AMI was anteroseptal in 181 (33.5%) and inferior/posterior in 267 (49.5%) of the patients. The AMI was Q wave in type in 279 (51.7%) of the patients. At discharge 410 (80.4%) were on beta-adrenergic blocking agents, and 212 (41.6%) of the patients were on angiotensin converting enzyme inhibitors. Only 55 patients (10.8%) were on calcium antagonists with 47.3% of these patients on a beta-blocker as well. Thirty patients died during their hospital stay with an in-hospital mortality rate of 5.6%. Coronary angiography was done in 135 (25%) patients with subsequent coronary angioplasty and bypass surgery done on 51 (9.4%) and 17 (3.1%) patients, respectively. The mean duration of hospital stay was 4.9 ± 0.1 days.

Of the 540 patients, 300 underwent a predischarge ET (55.6%). Of these, 216 (72.0%) underwent the ET within three days of their admission (i.e., within 72 h of the time recorded in the hospital legal admission form). Of the 216 patients, 73 (33.9%) underwent the ET within 48 h of admission, with 66.1% undergoing the test between 48 to 72 h of admission. The clinical characteristics and investigational data on these patients are outlined in Table 1. There were four patients with voltage criteria for left ventricular hypertrophy with nine patients that showed ST depression of >0.1 mV in the resting ECG. There were no patients with left bundle branch block. A significantly higher proportion of men (43.6%) were able to undergo the ET within 3 days compared with the women (32.1%, $p < 0.05$). The BPR was employed in 99.5% of the patients, with one patient undergoing an ET starting at stage II of the modified BPR in view of the uncertainty regarding the ability to start at stage I of the BPR. The mean duration of exercise was 6.7 ± 0.2 min with a range of 1.3 to 12 min. The exercise duration was significantly higher in the men ($p < 0.001$). Thirty-three patients (15.3%) completed more than 9 min of exercise (thus, reaching Stage IV of the BPR) with a further 76 patients (34.7%) completing over 6 min of exercise. The maximum heart rate attained was 116 ± 1.3 (range 64–163 beats/min) for the entire group with value being significantly higher in the men ($p < 0.05$). The maximum heart attained as a percentage of the predicted maximum heart rate for age had a mean of 72.2 ± 0.8%. At the time of the ET, 187 patients (86.6%) were on beta-blockers. The ET results were: positive in 56 (25.9%) patients, negative in 124 patients (57.4%), indeterminate in 36 patients (16.7%). Women had a higher incidence of indeterminate tests (28.3% vs. 12.9% for men). Subsequent exercise/persantine sestamibi scans were booked on nine patients (4.2%). Following the ET, 87 patients (40.3%) were discharged the same day, with another 73 patients (33.8%) discharged the following day (thus, 74.1% were discharged within 24 h).

Of the 56 patients with positive ET, 28 patients underwent coronary angiography before discharge with 11 and 3 patients requiring coronary angioplasty and coronary artery bypass surgery, respectively. Of the balance of 28 patients, 16 underwent coronary angiography as outpatients with 8 patients requiring coronary angioplasty and 1 patient referred for bypass surgery. Of the 36 patients with indeterminate tests, 12 patients underwent coronary angiography (10 as inpatients) with 6 patients requiring coronary angioplasty. Thus, 38 patients (17.6%) were scheduled to have coronary angiography as inpatients (after consideration of the ET results), and these patients had a more prolonged hospital stay.

The mean duration of hospital stay for the EETGP was 4.0 ± 0.1 days with the value higher for the women (4.5 ± 0.4 days) compared with the men (3.9 ± 0.2 days) although the difference did not achieve statistical significance ($p > 0.05$).

The ET was terminated due to: maximum effort in 89 patients (41.2%); worsening chest pain in 12 patients (5.6%); significant ST segment depression in 19 patients (8.8%); achievement of 90% of the predicted maximum heart rate in 6 patients (2.8%); a low level test (i.e., at the end of stage III or IV of the BPR as outlined in the Methods section) in 63 patients (29.2%); other reasons such

Table 1. Clinical and Exercise Test Data on the Early Exercise Test Group (n = 216; Mean ± Standard Error of the Mean or the Number of Patients, With Percentages Within that Group in Brackets)

	Men	Women
Number of Patients	**163**	**53**
Age (yrs)*	57.8 ± 0.9	63.2 ± 1.6
Day of Exercise Test		
Within 2 days	63 (38.7%)	10 (18.9%)
Third day	100 (61.3%)	43 (81.1%)
Exercise Duration (min)*	7.2 ± 0.2	5.0 ± 0.3
0–3 min	7 (4.3%)	10 (18.9%)
>3–6 min	56 (34.4%)	35 (66.0%)
>6–9 min	70 (42.9%)	5 (9.4%)
>9 min	30 (18.4%)	3 (5.7%)
Peak Heart Rate (beats/min)		
Achieved*	118 ± 2	111 ± 3
As % of predicted maximum	72.8 ± 0.9	70.7 ± 1.8
Exercise Test Results		
Positive	44 (27.0%)	12 (22.6%)
Negative	98 (60.2%)	26 (49.1%)
Indeterminate	21 (12.9%)	15 (28.3%)
Peak Creatine Kinase (u/l)	1492 ± 293	1176 ± 153
Duration of Hospital Stay (days)	3.9 ± 0.1	4.5 ± 0.4
Complications		
Prolonged pain/ST depression†	1 (0.6%)	0 (0.0%)
Drop in SBP	5 (3.1%)	2 (3.8%)
AMI/death/sustained VT	0 (0.0%)	0 (0.0%)
Nonsustained VT	1 (0.6%)	0 (0.0%)

*$p < 0.05$. †Chest pain or significant ST segment depression persisting for >5 min after exercise.

AMI = acute myocardial infarction; SBP = systolic blood pressure; VT = ventricular tachycardia.

Table 2. Demographic and Historical Data on the Six Groups of Patients (n = 540; Mean ± Standard Error of the Mean or the Number of Patients, With Percentages Within that Group in Brackets)

	EETGP	LETGP	NETGP	DECGP	CAGP	CABGP
No. of Patients	216 (40.0%)	84 (15.6%)	132 (24.4%)	29 (5.4%)	68 (12.6%)	11 (2.0%)
Age (yr)	59.0 ± 0.8	61.1 ± 1.4	74.6 ± 1.1	75.3 ± 2.1	62.8 ± 1.4	67.6 ± 2.7
Gender						
Women*	53 (24.5%)	32 (38.1%)	52 (39.4%)	13 (44.8%)	15 (22.1%)	1 (9.1%)
Men	163 (75.5%)	52 (61.9%)	80 (60.6%)	16 (55.2%)	53 (77.9%)	10 (90.9%)
Hypertension	80 (37.0%)	50 (59.5%)	73 (55.3%)	16 (55.2%)	35 (51.5%)	4 (36.4%)
Diabetes*	32 (14.8%)	20 (23.8%)	39 (29.5%)	5 (17.2%)	16 (23.5%)	2 (18.2%)
Known Dyslipidemia	79 (37.0%)	36 (43.0%)	43 (32.6%)	3 (10.3%)	29 (42.6%)	6 (54.5%)
F/H CAD	92 (42.6%)	25 (29.8%)	29 (22.0%)	8 (27.6%)	19 (27.9%)	5 (45.5%)
Smokers						
Current	89 (41.2%)	32 (38.1%)	34 (25.8%)	6 (20.7%)	25 (36.8%)	2 (18.2%)
Ever	154 (71.3%)	58 (69.0%)	84 (63.6%)	15 (51.7%)	56 (82.4%)	7 (63.6%)
History of						
CCF*	5 (2.3%)	4 (4.8%)	30 (22.7%)	8 (27.6%)	8 (11.8%)	0 (0.0%)
AMI*	42 (19.4%)	17 (20.2%)	55 (41.7%)	8 (27.6%)	27 (39.7%)	7 (63.6%)
Angina*	69 (31.9%)	36 (42.9%)	68 (51.5%)	14 (48.3%)	42 (61.8%)	9 (81.8%)
PTCA	8 (3.7%)	5 (6.0%)	7 (5.3%)	1 (3.4%)	9 (13.2%)	2 (18.2%)
Retirees*	84 (39.0%)	37 (44.0%)	100 (75.8%)	24 (82.8%)	33 (48.5%)	9 (81.8%)
BMI	29.3 ± 0.9	27.7 ± 0.8	27.0 ± 0.7	26.6 ± 2.5	28.2 ± 0.6	28.0 ± 1.0

*$p < 0.05$ for the F value in the analysis of variance; significant differences between the individual groups (by the least significant difference test) are outlined in the text.

AMI = acute myocardial infarction; BMI = body mass index; CABGP = coronary artery bypass surgery group; CAGP = coronary angiography/angioplasty group; CCF = congestive cardiac failure; DECGP = deceased group; EETGP = early exercise test group; F/H CAD = family history of coronary artery disease; LETGP = late exercise test group; NETGP = no exercise test group; PTCA = percutaneous transluminal coronary angioplasty.

as claudication, patient apprehension, presyncope in 26 patients (12%). Only one patient (0.5%) had the test terminated due to nonsustained ventricular tachycardia. There were no deaths, cardiac arrests, myocardial infarctions or sustained ventricular tachycardias related to the ETs. There were seven patients (3.2%) who had a drop in systolic blood pressure >10 mm Hg during test, five patients (2.3%) with persistent (lasting >5 min after termination of ET) ST segment depression, one patient (0.6%) who had prolonged angina (lasting >5 min after termination of ET) and one patient (0.6%) who had transient third degree heart block as a result of the test.

Comparative data for the five groups of patients outlined in the Methods section are tabulated in Tables 2 and 3. The EETGP had a significantly lower maximum creatine kinase value, a shorter length of hospital stay and a lower percentage of women and diabetics compared with the LETGP ($p < 0.05$). The LETGP had a higher incidence of anteroseptal AMIs, thrombolytic therapy, congestive cardiac failure, artificial ventilation, continuing angina and sustained ventricular tachycardia/ventricular fibrillation compared with the EETGP ($p < 0.05$). The NETGP and the DECGP had a higher mean age and a higher incidence of congestive cardiac failure and retired individuals compared with the other groups. The DECGP had a higher incidence of complications such as cardiogenic shock, sustained ventricular tachycardia/ventricular fibrillation, third degree heart block, need for mechanical ventilation and inotropic agents compared with all other groups.

Follow-up information at six weeks after discharge using a structured questionnaire was available on 492 (96.3%) of the 510 patients' discharged alive (Table 4). Of the 18 patients who could not be directly contacted/refused to participate in the follow-up assessment, 13 patients were known to be alive at six weeks after discharge (as per information from the family physician's office). Thus, only five patients (0.98%) were lost to follow-up (reasons = out of country patients, movement out of province with no contact telephone number or address available). Unscheduled return visits, emergency room visits and readmissions were not significantly different between the groups ($p > 0.05$). During this period, unscheduled return visits occurred in 22.7% and 26.5% of the EETGP and LETGP, respectively. Readmissions were lower (although not statistically significant) and visits to the emergency department similar in the EETGP compared with the LETGP. In the EETGP 45.4% of the patients who were employed at the time of the AMI had returned to work within six weeks (of the AMI) compared with only 27.6% of the LETGP. However, this difference was not statistically significant ($p > 0.05$).

Follow-up information at one year after discharge is outlined in Table 4. This information was available for 484 (97.4%) of the 497 eligible patients: that is, 540—30 (died before discharge)—13 (has not reached one year yet). Thus, 13 patients were lost to follow-up. The NETGP had a 34.9% incidence of death during this period compared with 4.0% and 8.8% incidences in the EETGP and LETGP,

Table 3. Clinical and Investigational Data on the Six Groups of Patients (n = 540; Mean ± Standard Error of the Mean or the Number of Patients, With Percentages Within that Group in Brackets)

	EEGTP	LETGP	NETGP	DECGP	CAGP	CABGP
No. of Patients	216 (40.0%)	84 (15.6%)	132 (24.4%)	29 (5.4%)	68 (12.6%)	11 (2.0%)
Location of AMI						
Anteroseptal*	50 (23.1%)	37 (44.0%)	48 (36.4%)	14 (48.3%)	28 (41.2%)	4 (36.4%)
Inferior/posterior	133 (61.6%)	36 (42.9%)	50 (37.9%)	10 (34.5%)	32 (47.1%)	6 (54.4%)
Lateral	27 (12.5%)	8 (9.5%)	19 (14.4%)	3 (10.3%)	7 (10.3%)	1 (9.1%)
Indeterminate	6 (2.8%)	3 (3.6%)	15 (11.4%)	2 (6.9%)	1 (1.5%)	0 (0.0%)
Type of MI						
Q wave	119 (55.1%)	54 (64.3%)	57 (43.2%)	16 (55.2%)	31 (45.6%)	2 (18.2%)
Non-Q wave	97 (44.9%)	30 (35.7%)	75 (56.8%)	13 (44.8%)	37 (54.4%)	9 (81.8%)
Maximum CK (u/l)	1441 ± 225	1918 ± 209	1544 ± 147	3408 ± 1017	1307 ± 252	642 ± 141
Duration of hospital stay (days)	4.0 ± 0.1	5.8 ± 0.2	4.9 ± 0.2	2.8 ± 0.7	6.2 ± 0.4	12.9 ± 1.4
Thrombolysis*	96 (44.4%)	52 (61.9%)	40 (30.3%)	6 (20.7%)	17 (25.0%)	5 (45.5%)
Complications						
Deaths	0 (0.0%)	1 (1.2%)	0 (0.0%)	29 (100%)	0 (0.0%)	0 (0.0%)
CCF*	6 (2.8%)	17 (20.2%)	47 (35.6%)	17 (58.6%)	14 (20.0%)	1 (9.1%)
Cardiogenic shock	0 (0.0%)	0 (0.0%)	6 (4.5%)	11 (37.9%)	5 (7.4%)	0 (0.0%)
Sustained VT/VF*	5 (2.3%)	7 (8.3%)	11 (8.3%)	8 (27.6%)	6 (8.8%)	0 (0.0%)
3° Heart block	5 (2.3%)	2 (2.4%)	9 (6.8%)	6 (20.7%)	4 (5.9%)	0 (0.0%)
Recurrent angina*	30 (13.9%)	20 (23.8%)	24 (18.2%)	4 (13.8%)	22 (32.4%)	4 (36.4%)
Artificial ventilation*	0 (0.0%)	4 (4.8%)	12 (9.1%)	19 (65.5%)	5 (7.4%)	0 (0.0%)
Atrial arrhythmia*	7 (3.2%)	9 (10.7%)	19 (14.4%)	6 (20.7%)	3 (4.4%)	1 (9.1%)
Cardiac arrest*	2 (0.9%)	4 (4.8%)	6 (4.5%)	18 (62.1%)	3 (4.4%)	0 (0.0%)
Coronary angiography	39 (18.1%)	17 (20.2%)	0 (0.0%)	3 (10.3%)	68 (100%)	11 (100%)
Inotropic agents	0 (0.0%)	5 (6.0%)	10 (7.6%)	14 (48.3%)	6 (8.8%)	1 (9.1%)
PTCA	14 (6.5%)	7 (8.3%)	0 (0.0%)	2 (6.9%)	28 (41.2%)	0 (0.0%)
ET maximum HR (beats/min)	116 ± 1.7	114 ± 2.0	—	—	—	—

*$p < 0.05$ for the F value in the analysis of variance; significant differences between the individual groups (by the least significant differences test) are outlined in the text.

CABGP = coronary artery bypass surgery group; CAGP = coronary angiography/angioplasty group; CCF = congestive cardiac failure; CK = creatine kinase; EETGP = early exercise test group; ET = exercise test; HR = heart rate; LETGP = late exercise test group; NETGP = no exercise test group; PTCA = percutaneous transluminal coronary angiography; VT = ventricular tachycardia; VF = ventricular fibrillation.

respectively ($p < 0.001$). The incidences of death in the EETGP and LETGP were not significantly different ($p > 0.05$). The occurrence of congestive cardiac failure was also significantly higher in the NETGP (12.9%) compared with the EETGP (1.1%) and LETGP (4.2%) ($p < 0.001$). However, the incidence of unstable angina and recurrent AMI in the NETGP was not significantly different. The EETGP appeared to have a slightly lower incidence of death, unstable angina, congestive cardiac failure and coronary angioplasty during the year after discharge compared with the LETGP although no statistically significant difference was demonstrated.

Discriminant function analysis done with each variable entered in a stepwise manner revealed in-hospital congestive cardiac failure; the ET groups (as identified in this study) and the age of the patient were the only significant independent predictors of death within one year on those discharged alive. The standardized canonical discriminant function coefficients for congestive cardiac failure, ET group and age were 0.594, 0.516 and 0.247, respectively. The canonical correlation coefficient for the discriminant function was 0.424. The "Jack-knife" method correctly classified 76.4% of the patients.

DISCUSSION

This study examined the feasibility and safety of doing ET using the BPR early on after an AMI while the patients are still within the CICU. The study demonstrated that early ETs could be performed in approximately 40% of the patients admitted with an AMI. If the patients who died and those who underwent early coronary angiography due to continuing angina were excluded (as the ET was deliberately omitted in the latter group although it could have been done with an anticipated lower incidence of complications given the prior revascularization), the percentage who underwent early ET would constitute 50.0% of the total population. Further, the EETGP constituted 72.0% of the total number of patients who underwent ET before discharge. Very few complications were noted in spite of the BPR being used in almost all instances with the patients exercising to the end of stage III/IV of the protocol (depending on the age) in the absence of other end points.

Previous studies of early ET with AMI. Review of the literature revealed only a few investigations looking at ET within the first three days after myocardial infarction or using symptom limited ETs during this early period. A

Table 4. Follow-up Information on the Patients Discharged Alive (n = 510; the Number of Patients, With Percentages Within that Group in Brackets)

	EETGP	LETGP	NETGP	CAGP	CABGP
No. of Patients	216 (42.3%)	83 (16.3%)	132 (25.9%)	68 (13.3%)	11 (2.2%)
Discharge Medications					
Ace-inhibitor*	69 (31.9%)	46 (55.4%)	65 (49.2%)	28 (41.2%)	4 (36.4%)
Beta-blockers	187 (86.6%)	77 (92.8%)	81 (61.4%)	57 (83.8%)	8 (72.7%)
Calcium antagonist	18 (8.3%)	3 (3.6%)	25 (18.9%)	6 (8.8%)	3 (27.3%)
Six-week Follow-up					
Unscheduled return visits	49 (22.7%)	22 (26.5%)	32 (24.2%)	23 (33.8%)	2 (18.2%)
Readmissions	19 (8.8%)	12 (14.5%)	20 (15.1%)	6 (8.8%)	0 (0.0%)
Emergency room visits	26 (12.0%)	11 (13.2%)	9 (6.8%)	14 (20.6%)	2 (18.2%)
Return to work†	45.4% (40/88)	27.6% (8/29)	INS	23.5% (4/17)	INS
One-Year Follow-up**					
Death*	4.0%	8.8%	34.9%	15.4%	9.1%
Unstable angina	4.9%	6.9%	10.8%	10.5%	9.1%
Recurrent MI	4.9%	7.0%	9.6%	7.0%	0.0%
Cardiac failure*	1.1%	4.2%	12.9%	5.3%	0.0%
Coronary angioplasty	6.4%	9.8%	5.5%	7.1%	0.0%

*$p < 0.05$ for the F value in the analyses of variance. Significant differences between the individual groups (using the Bonferonni's intervals) are outlined in the text. †On those employed at admission.

CABGP = coronary artery bypass surgery group; CAGP = coronary angiography/angioplasty group; EETGP = early exercise test group; INS = insufficient number of patients employed at time of admission for meaningful data (NETGP = 9 patients, CABGP = 1 patient); LETGP = late exercise test group; NETGP = no exercise test group.

**One-year follow-up was available on 484 of the 497 eligible patients, that is, 540—30 (died before discharge)—13 (not reached one-year yet) = 497.

study by Juneau et al. (12) compared symptom limited ETs versus a low level test on 202 patients with an AMI. The symptom limited stress test demonstrated ischemia in 89 of 202 (44.1%) patients while the low level test demonstrated ischemia in only 56 of 202 (27.7%) patients. The 202 patients included in the above study represented 41% of the 495 patients who survived to hospital discharge. In this study a similar percentage (40.0%) of patients who survived to hospital discharge underwent an ET using the BPR within three days of admission. In contrast, in the study by Juneau et al. (12), the test was done at a mean of 7.4 ± 2.3 days after the AMI. In addition, a Stanford modification of the Naughton protocol rather than a BPR was used in that study even for the symptom limited test. A study by Topol et al. (8) looked at 126 patients who underwent an ET on day 3 after an AMI. These 126 patients were from a group of 507 patients admitted with an AMI with 195 patients undergoing coronary angioplasty. Of the 126 patients more than 94 patients (74.6%) had undergone prior coronary angiography with angioplasty performed in 64.4% of those undergoing angiography. This study used a submaximal ET with concomitant thallium scintigraphy with termination of the test at a heart rate of 140 beats/min. In this study, 30 patients (13.9%) achieved a maximum heart rate of >140 with 33 patients (15.7%) exercising beyond stage III of the BPR. The study by Topol et al. (8) randomized 80 of the patients with negative ET to early (day 3) discharge versus the conventional 7–10 day discharge. The study demonstrated no significant adverse outcomes from the early discharge. In this study 40.3% of the patients were discharged home the same day after the early ET with another 33.8% discharged the next day. Further, the adoption of early ET while the patients are still in the CICU has resulted in shortening of the in-hospital stay for AMI as demonstrated in a recent study from this institution (9). The mean length of stay for AMI was 5.1 days in this study (9) with 53% of the patients directly discharged from the CICU within 4 days. Several other studies have demonstrated the usefulness of ET in patients with unstable angina or AMI although the ETs were performed much later in the hospital course (5–14 days after admission) or using less intense protocols (13,14).

Safety concerns with early ET. The reason for avoiding early ET after AMIs generally appears to be related to the concern regarding safety. This study demonstrated that immediate complications related to the ET were negligible with almost all adverse effects being reversible and transient when patients are selected based on their clinical course in the CICU. Thus, acute myocardial rupture, a complication that is possible and probably fatal when it occurs, was not observed in this study. However, the occurrence of myocardial rupture during an ET would still remain a possibility and a concern when large numbers of patients are tested early using a BPR as this study was limited to only 216 patients. Nevertheless, these serious events occur after AMIs in a minority of individuals even without exercise. Only a randomized control study comparing early versus late ET using the BPR would resolve the above issue if early ET would result in or predispose to cardiac rupture. As the incidence of cardiac rupture is very small, it is unlikely that such a study would ever be conducted due to the requirement of a very large number of patients. Cardiac rupture during exercise may be more likely to occur with larger

infarctions. In this study the EETGP had a mean creatine kinase peak, which was significantly less than that for LETGP. This suggests an appropriate clinical decision by the attending cardiologist who deemed patients with large AMIs to be not "ready" for ET as early as the patients with smaller myocardial infarctions. Nevertheless, the mean creatine kinase peak of 1441 ± 225 u/l for the EETGP suggests that this group did not constitute a population with very small infarctions. Further, even with a large AMI, delaying the ET by two to three days may not necessarily result in reduction in the incidence of myocardial rupture.

Data from a questionnaire dealing with 151,949 ETs done at 193 institutions within four weeks of an AMI revealed a mortality rate of 0.03% (fatal AMI, fatal cardiac arrest or rupture), a major nonfatal adverse event (nonfatal AMI or resuscitated cardiac arrest) rate of 0.09% and a minor complication rate of 1.5% (15). Thus, a small but definite incidence of serious complications will be expected with ET after an AMI, even when the test is delayed to a much later time.

Another complication that should be considered with ET using an aggressive protocol would be the development of ventricular aneurysms precipitated by infarct expansion due to the higher systolic blood pressures and heart rates attained during exercise. In the study by Topol et al. (8), no ventricular aneurysms were noted during a follow-up period on those who underwent ET at day 3. However, this study used a submaximal ET. The expected risk of precipitating aneurysm formation is low, as ET results in an increased systolic blood pressure and heart rate only for a very short period of time. The development of ventricular aneurysms are more likely influenced by persistent tachycardia and hypertension. Nevertheless, whether early ET using an aggressive protocol, such as the BPR, results in worsening of infarct expansion can only be determined by a randomized trial.

Advantages of early ET. These are several:

1) the patients with positive tests for ischemia could be selected for early coronary angiography (to consider revascularization) thereby shortening their ultimate length of stay,
2) those with negative tests for ischemia can be discharged home without further delay reducing overall hospital costs associated with the management of the myocardial infarction,
3) the higher levels of exercise attained with the BPR in younger patients would give them a greater sense of confidence in terms of returning to regular activities at home and work over the ensuing weeks.

The use of the modified Bruce/Naughton protocols for predischarge ET with the test terminated at 5–6 metabolic equivalent of time may impart a sense of apprehension in patients who felt exercise had to be limited to very low levels after discharge. This was especially so in the case of patients who were physically active in terms of regular exercise before the AMI. In the present institution, individuals with small/moderate AMIs who are able to complete stage II of the BPR are started on cardiac rehabilitation exercise programs within two weeks of the myocardial infarction enabling them to return to full-time work much earlier than previously. In this study 45.4% of the patients (who were employed at the time of admission) had returned to work within six weeks of the onset of the AMI.

Follow-up data. As demonstrated, early ET did not appear to result in any increase of unscheduled return visits (to family doctor, medicenter or emergency department) or readmissions within a six-week period after discharge; the rates for these events remained the same or lower as compared with the LETGP. However, as the EETGP and LETGP are two separate populations, one cannot exclude the possibility of an increase in these events by early exercise testing. This study is limited in this respect being observational in nature and not a randomized trial of early ET versus late ET or early ET versus no ET. However, such a randomized trial is unlikely to be performed (at least in Canada) given the current economic constraints. During the ensuing year there appeared to be a trend towards a lower incidence of coronary events (including death, unstable angina, development of congestive cardiac failure and the need for coronary angioplasty) as expected in the EETGP compared with the LETGP given the smaller size of the AMIs in the former group. However, recurrent AMI rate appeared to be similar or higher in the EETGP paralleling the higher percentage of non-Q AMIs in the EETGP.

This study confirms the high in-hospital as well as longer-term morbidity and mortality of the group of patients unable to undergo a predischarge ET (NETGP in this study) as has been shown previously (7). This is in spite of the fact that their infarct size did not appear to be larger based on the creatine kinase peak of 1544 ± 147 U/l compared with the EETGP (1441 ± 225 U/l, $p > 0.05$). The NETGP were an older group of patients with a higher percentage of non–Q myocardial infarctions. Further, the inability to perform an ET in their group was not related to ongoing angina but rather to physical limitations. This study suggests that special emphasis should be placed on the NEGTP to minimize the occurrence of future coronary events. Pharmacologic-stress imaging in this group of patients will likely help to further risk stratify, by identifying those with reversibly ischemia. However, it remains to be proven whether coronary angiography with revascularization, performed when indicated and feasible, would alter the prognosis in a favorable manner as the risks of intervention are also likely going to be higher in this group of older patients with physical limitations. In this regard it is interesting that the NETGP did not demonstrate a significantly higher incidence of re-infarction and the occurrence of unstable angina compared with the other groups, while demonstrating a higher incidence of the occurrence of

congestive cardiac failure. This may suggest that the higher mortality may be related to impaired left ventricular function rather than ischemic events. Further, the higher mortality is likely, at least partly, related to concurrent illnesses, which may not be easily amendable to disease modification.

Conclusions. In summary, this study demonstrates that ET within two to three days of an AMI (without discontinuation of beta-blocker, if already commenced) is a feasible and safe strategy in a significant proportion of patients admitted with a myocardial infarction. This could lead to early triage with expected cost savings.

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